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HPLC in the Pharmaceutical Industry

Preface

Although modern high performance liquid chromatography (HPLC) became popular in 1969, it was not widely accepted by pharmaceutical analysts until several years later. Four types of chromatography (namely, column, gas, paper, and thin layer) had been well established and officially employed in the isolations and assays of drugs as described in the United States Pharmacopeia (USP). However, the usefulness of HPLC techniques for pharmaceutical analysis was not appreciated by many practitioners in the pharmaceutical industry until the first HPLC systems capable of quantitative analysis became commercially available.

The acceptance of HPLC over gas chromatography in pharmaceutical analysis is mainly due to its improved selectivity and efficiency in separating nonvolatile organic drug molecules. Gas chromatographic techniques normally require a chemical derivatization step prior to the analysis of the drug, and chemical modifications of an organic drug molecule are undesirable in the stability studies of drug substances and drug products. HPLC techniques, on the other hand, offer enhanced detection sensitivity, improved accuracy, and reproducibility of drug analysis in the course of drug research, development, and quality control testing of marketed drug products. Many HPLC methods have been developed as the preferred methods for monitoring drug stability, identity of drug and other components, impurities, and degradation products of new chemical entities (NCE) or new molecular entities. The term "new molecular entities" has been used in the last several years when peptide and protein drugs discovered via biotechnology routes have been included. On the other hand, many wet chemistry and classical test methods for existing drug products have also been replaced by HPLC methods for more accurate measurements, better precision, and much faster analytical run time. This translates into lower cost per test in R&D and QC laboratories.

Automation, integrating HPLC with powerful data acquisition and reduction systems, and laboratory robotics have further improved the precision and accuracy of drug analysis by HPLC. Recognizing the reliability of the technique, both the phar-

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maceutical industry (as represented by such trade association as the Pharmaceutical Manufacturers Association [PMA]) and the regulatory agencies (such as the Food and Drug Administration [FDA]) have endorsed HPLC as the preferred methodology for testing drug samples. Indeed, PMA has drafted guidelines for the validation of HPLC methods intended for the assays of drugs and related compounds. FDA has been raising its standards of acceptable test results as scientific advances in the field of drug analysis move rapidly forward. Automated HPLC systems have been indispensable for any laboratories charged with the mandate of producing results that meet the "quality and quantity" standard set by company management.

This volume, composed of a total of 11 chapters grouped into four parts, was written by 18 experts in the field. Part One, Contemporary LC Techniques in Pharmaceutical Analysis, reviews the use of microbore and high speed LC and column switching techniques for a wide range of drugs. Part Two, Specialized Detection Techniques, covers electrochemical, radiochemical, and computerized diode array detection and HPLC/Fourier transform infrared (FTIR) for the analysis of drugs and their degradation products in formulations, and drugs and their metabolites in biological fluids. Part Three, Automation in Pharmaceutical Analysis, surveys the application of HPLC to the dissolution of solid dosage forms and robotic automation of HPLC. Part Four, HPLC of Peptides, Proteins, and Enantiomeric Drugs, includes the analysis of new drug substances and enantiomeric drugs using chiral HPLC techniques, and the characterization of peptide and protein drugs by HPLC.

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